



E1833  
JACC March 12, 2013  
Volume 61, Issue 10



## TCT@ACC-i2: Invasive and Interventional Cardiology

### ALLOGENEIC CARDIOSPHERE-DERIVED CELLS AFTER REPERFUSION ARE EFFECTIVE IN REDUCING INFARCT SIZE AND ATTENUATING ADVERSE REMODELING IN PIGS WITH ACUTE MYOCARDIAL INFARCTION

Poster Contributions

Poster Sessions, Expo North

Sunday, March 10, 2013, 3:45 p.m.-4:30 p.m.

---

Session Title: Preclinical and Translational Research

Abstract Category: 52. TCT@ACC-i2: Translation and Pre-clinical Research

Presentation Number: 2111-245

---

Authors: Hideaki Kanazawa, Konstantinos Malliaras, Kristine Yee, James Dawkins, Eleni Tseliou, Linda Marban, Rajendra Makkar, Eduardo Marban, Cedars-Sinai Medical Center, Los Angeles, CA, USA

**Background:** Both autologous and allogeneic cardiosphere-derived cells (CDCs) have proven safe and effective in chronic ischemic cardiomyopathy in pig model with chronic ischemic cardiomyopathy. However, administration of allo-CDCs immediately after reperfusion in pigs with acute MI has not been assessed. We first aimed to establish an optimal dosage for CDCs in acute MI to test safety and efficacy. Second, we performed a placebo-controlled pivotal study for long-term evaluation.

**Methods:** Mini-pigs underwent 1.5h mid-LAD balloon occlusion and reperfusion. First, total 15 mini-pigs received escalating doses (5, 7.5 and 10M cells) of allo-CDCs to find optimal dosage. Forty-eight hours later, left ventriculography (LVG) was performed and pigs were sacrificed to measure area at risk (AAR) and infarct size (IS). The maximal safe cell dosage (~7.5M) or vehicle were infused into LAD of mini-pigs (n=8 each). Pigs underwent cardiac MRI after cell infusion and 8 weeks later to evaluate efficacy.

**Results:** In the systematic dose-escalation study, there were no deaths in any arms. 7.5M allo-CDCs infusion significantly decreased infarct size and LV end-diastolic volume two days after intervention compared with placebo infused pigs without any concerns. In the efficacy study, although the ejection fraction (EF), LV end-diastolic and systolic volume index (LVEDVI and ESVI) were equivalent in both groups by LVG before intervention, the EF by MRI after CDC infusion was significantly higher than the placebo pigs (EF:  $54.1 \pm 3.8\%$  vs  $49.6 \pm 4.1\%$ ,  $p=0.036$ ). Moreover, the acute remodeling just 1hr after intervention was significantly attenuated in CDC-treated pigs compared with placebo pigs (LVEDVI:  $54 \pm 5$  vs  $63 \pm 9$  ml/m<sup>2</sup>,  $p=0.016$ , ESVI  $25 \pm 3$  vs  $32 \pm 5$  ml/m<sup>2</sup>,  $p=0.003$ ). In terms of long-term efficacy, there is a trend to decrease the LVESVI at 8 weeks post infusion compared with placebo groups ( $33 \pm 9$  vs  $43 \pm 10$  ml/m<sup>2</sup>,  $p=0.26$ ).

**Conclusions:** Allo-CDCs infusion promptly after reperfusion is safe and attenuates remodeling with optimal dosage in pig with AMI. The present results support the development of allo-CDCs as adjunctive therapy for AMI in humans.